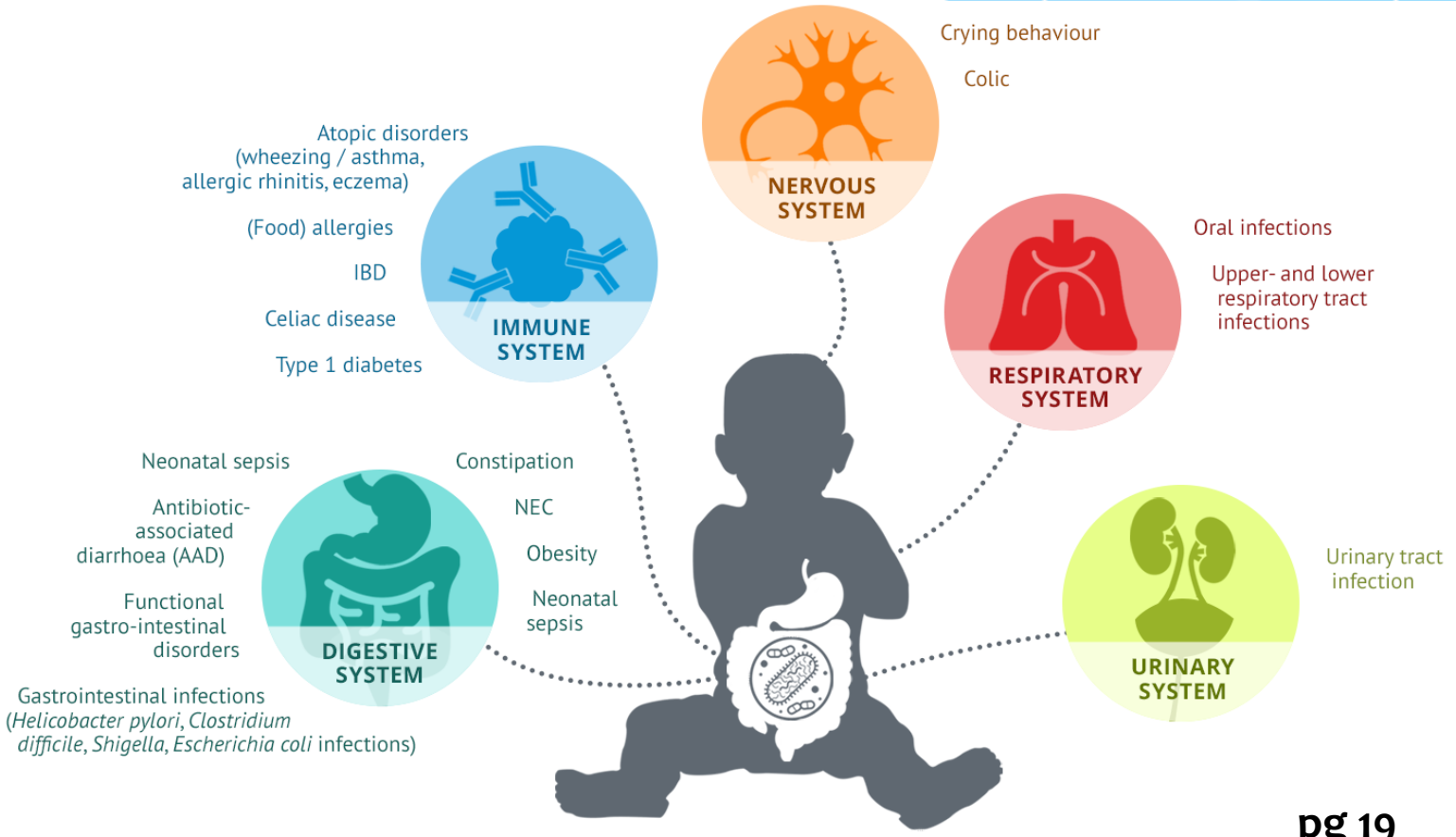
Microbiota in health and disease:
from pregnancy to childhood

Pamela Browne, arts-onderzoeker
21 september 2017

1e kindermicrobiota boek ter wereld



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Chapter 6	Pamela Browne/Eva van den Berg/Carolina de Weerth
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Chapter 13	Valerie Sung/Anna Klein
Chapter 14	Marc Benninga/Louis Akkermans/Marit Vinck
Chapter 15	Tim de Meij
Chapter 16	Coline Gerritsen/Jesse Younes
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Boek indeling

* **Zwangerschap – 12 jaar**
* **17 hoofdstukken**
  * Deel 1: introductie
  * Deel 2: ‘influencing factors’
  * Deel 3: ‘microbiota en (ontwikkeling van) fysiologische systemen’
    * Darmstelsel, immunologisch, neurologisch
  * Deel 4-6: de rol van microbiota bij kinderziekten en gedrag
  * Deel 7: microbiota analyses
  * Deel 8: pre- probiotica en synbiotica

Part I. THE INFANT AND CHILD MICROBIOTA

1 Infant and Child Microbiota: current state and future research

Pamela D. Browne, Eric Claassen

Chapter 1 brings together recent insights paediatric microbiome research and summarizes future directions for research in this field.

Part II. SHAPING THE GUT: ENVIRONMENTAL FACTORS AFFECTING INFANT MICROBIAL DEVELOPMENT

2 Development of the neonatal microbiota

Gregory R. Young, Stefan Zalewski, Stephen P. Cummings, Clare Lanyon

In chapter 2, the authors reflect upon the development gut microbiota during infancy, identify possible causes of bacterial dysbiosis within the neonatal gut and explain associated diseases, including NEC, neonatal sepsis and antibiotic associated

3 Maternal factors influencing development of the infant microbiota

Pamela D. Browne, Eva van den Berg, Eric Claassen, Carolina de Weerth

Chapter 3 reviews the associations between prenatal maternal stress, maternal obesity and diabetes and the development of the infant gut microbiota, and additionally identifies the implications on child health.

4 The impact of pre and postnatal interventions on infant gut microbiota

Anita Kozyrskyj, Mon Tun

Examples in chapter 4 offer focus on gut microbial impact of four medical interventions: caesarean delivery, maternal intrapartum antibiotic prophylaxis, hospitalization post birth and postnatal infant antibiotic treatment.

5 Early diet and the infant gut microbiome

John Penders

In chapter 5, the author discusses how the infant microbiome is shaped by breastfeeding and solid foods.

Part III. A CROSSTALK BETWEEN HUMAN MICROBIOTA AND PHYSIOLOGICAL SYSTEMS

6 The intestinal microbiota and the child's immune system

Maria C. Jenmalm, Susan L. Prescott

In chapter 6, the authors demonstrate how the intestinal microbiota is involved in the maturation of a balanced postnatal innate and adaptive immune system.

7 Interactions between intestinal microbiota and the gastrointestinal system

Carlos Gómez-Gallego, Seppo Salminen

In this chapter, the authors explore how gut microbiota composition and its metabolites affect gastrointestinal development and functioning in early life.

8 The interplay between the microbiota and the central nervous system during neurodevelopment

Aadil Bharwani, John Bienenstock, Paul Forsythe

In chapter 8, the authors offer perspectives on the role of gut bacteria in development of the hypothalamus-pituitary-adrenal (HPA) axis, central and enteric nervous systems during early life.

Part IV. GUT MICROBIOTA: ITS ROLE IN PAEDIATRIC DISEASES

9 The role of intestinal microbiota in infant allergic diseases

Hania Szajewska

In chapter 9, the author discusses the role of the gut microbiota in the development of allergic diseases typically found in infants, and reviews the role of pre- and probiotics for prevention and treatment.

10 Intestinal microbiota and allergic and auto-immune disorders in children

Tim de Meij

In chapter 10, the authors provide an overview of the role of gut microbiota in aetiology of auto-immune diseases and atopic disorders in children and present potential benefits of preventive and therapeutic microbiota-based interventions.

11 Intestinal microbiota and the development of gastrointestinal disorders in children

Marc A. Benninga, Marti Vink, L.M.A. Akkermans

Authors present in chapter 11 the association between aberrant gut microbiota and functional gastrointestinal disorders and infections, constipation and obesity in children and discuss therapeutic strategies to manipulate the microbiota composition.

Part V. FROM BOWEL TO INFANT BEHAVIOUR

12 The association between intestinal microbiota and infant crying and behaviour

Valerie Sung, Anna Partty

In chapter 12, the authors outline the association between intestinal microbiota, use of probiotics and infant crying and behaviour, with particular focus on infant colic.

Part VI. CONSEQUENCES OF DYSBIOSIS OUTSIDE OF THE GUT AND CHILDHOOD DISEASES

13 Microbiota and the respiratory tract

Jessica A. Younes, Jacoline Gerritsen

In chapter 13, the authors share insights in the role of microbial dysbiosis and associated biofilms in acute respiratory tract infections, dental caries, periodontal disease, and oral candidiasis in infants and children.

14 Microbiota and the urinary system

Jessica A. Younes, Jacoline Gerritsen

In chapter 14, the authors offer perspectives on newly discovered urinary microbiome and provide suggestions to optimize urinary microbiome research in paediatric populations.

Part VII. ASSESSMENT OF MICROBIOTA

15 Methodologies for microbiota assessment in infancy and childhood

D. Radjabzadeh, Sergey R. Konstantinov, Henriette A. Moll, André G. Uitterlinden, Erwin G. Zoetendal, Robert Kraaij

In chapter 15, the authors provide an overview of different microbial analysis techniques and deliver information to help design good quality clinical studies.

Part VIII. MANIPULATING THE GUT MICROBIOTA

16 Probiotic interventions to optimize the infant and child microbiota

Yvan Vandenplas, Koen Huysentruyt

In Chapter 16, the authors consider the variety of pre-, pro- and synbiotics and discuss application and efficacy of these food supplements in various paediatric diseases.

17 Safety of probiotics

Maurits van den Nieuwboer, Pamela D. Browne, Eric Claassen

In chapter 17, the authors provide information on tolerability and safety of probiotic use in infants and children.

2

Development of the neonatal microbiota

Gregory R. Young, Stefan Zalewski, Stephen P. Cummings, Clare Lanyon

Key points:

- 1e 18 maanden van groot belang
  - Lage diversiteit, lage stabiliteit
- Functies
  - Stimuleren immuunsysteem
  - Produceren vitaminen
  - Vertering voedingsstoffen, opname
  - Barrière ziekteverwekkers (competitie)
  - Bevorderen darmwand/epitheel (barrière functie)
    - Melkzuurbacteriën (Lactobacillen, bifidobacteria)
- 'Critical window of development'
  - 0-2 jaar: ontwikkeling microbiota + lichaamsfuncties

Development of the neonatal microbiota

Gregory R. Young, Stefan Zalewski, Stephen P. Cummings, Clare Lanyon

Key points:

- **Dysbiose**
  1. 'Loss of key stone taxa' (bv. na AB, opgevulling pathogenen)
  2. 'Pathogenic taxa blooms'
  3. Reductie in diversiteit
  4. 'Functional shift' (bv. BM bifidobacterien naar vezel metaboliserende *Bacteroides*)

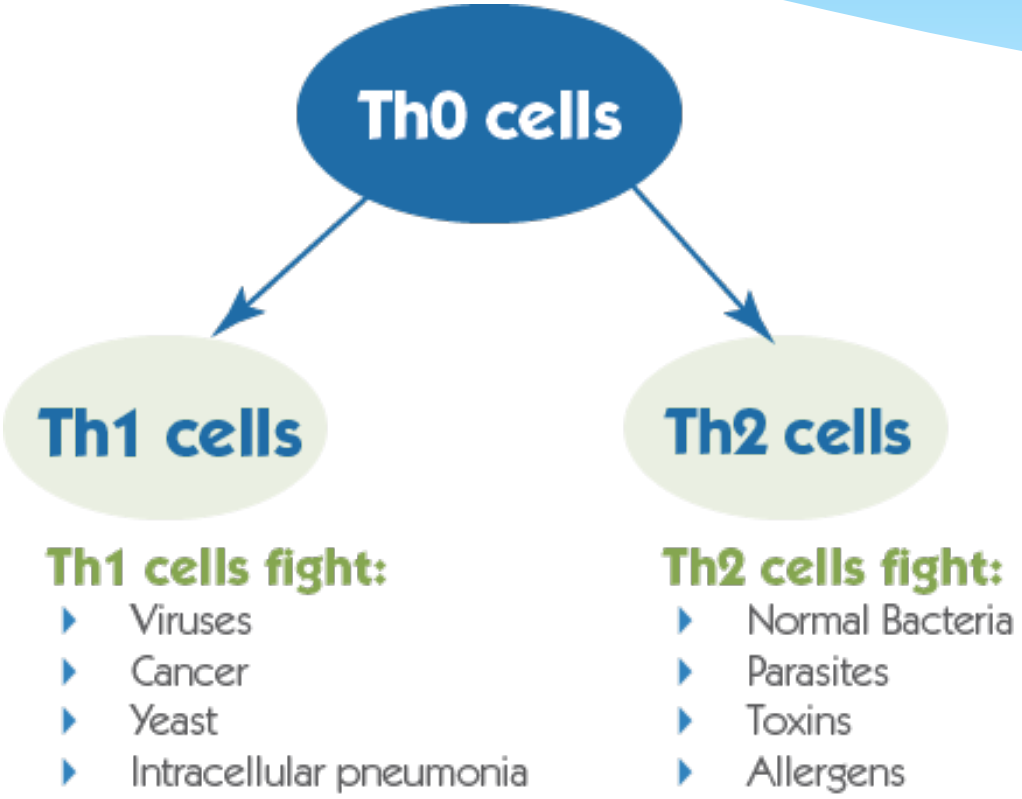
- **NEC (mortaliteit: 20-30% VLB <1500 gr met NEC)**
  1 en 2. + *Clostridium, Enterobacteriaceae, Escherichia*
  1 en 3. - AB gebruik
  - + BV, probiotica

- **AAD (5-30% gehospilatiseerde pten)**
  - *C. difficile* (10-20%)
  - Metronidazol, probiotica

2

Development of the neonatal microbiota

Gregory R. Young, Stefan Zalewski, Stephen P. Cummings, Clare Lanyon



IgA

IgE

Key points:

A terme, vaginaal, BV

- *Enterobactericeae, Escherichia, Lactobacillus* → <O2 → *Bifidobacterium*
- Th1 cel stimulatie

Prematuur, keizersnede

- *Staphylococcus, Enterobacteriaceae, Clostridium* → ~~*Bifidobacterium*~~
- Th2 cel stimulatie

2

Development of the neonatal microbiota

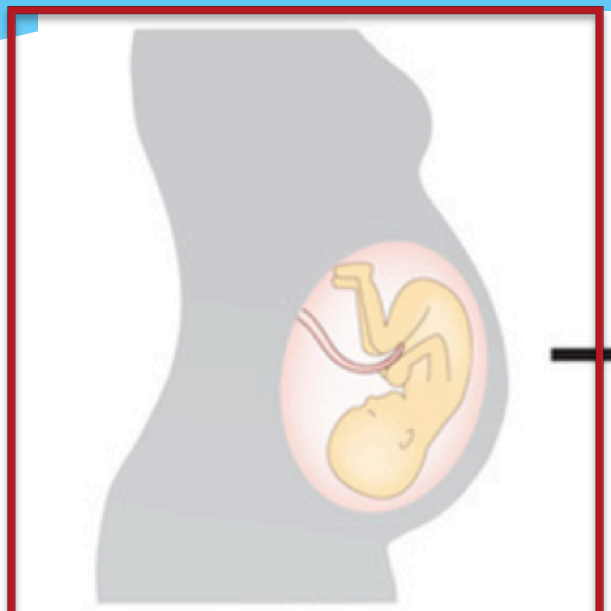
Gregory R. Young, Stefan Zalewski, Stephen P. Cummings, Clare Lanyon

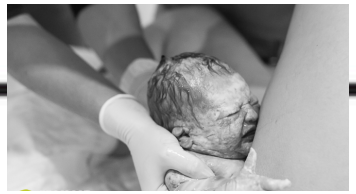
- **Vaginal seeding**
  - Te weinig bekend

3

Maternal factors influencing development of the infant microbiota

Pamela D. Browne, Eva van den Berg, Eric Claassen, Carolina de Weerth





Moment 1: Zwangerschap

Stress, gewicht, voeding, antibiotica

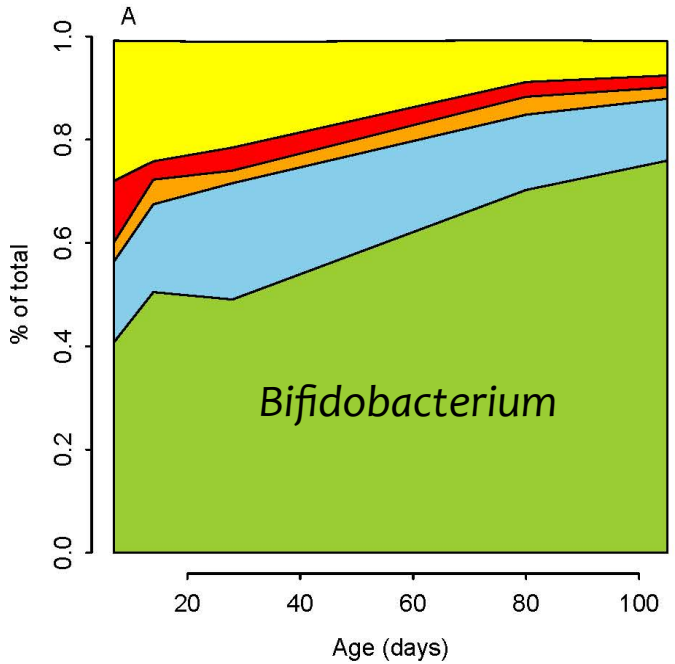
Moment 2: Geboorte

Keizersnede, vaginaal bevallen thuis, ziekenhuis, (leeftijd, gewicht)

Moment 3: 1e levensjaren

Voeding, antibiotica, familie omgeving (genen)

Zwangerschap: maternale stress

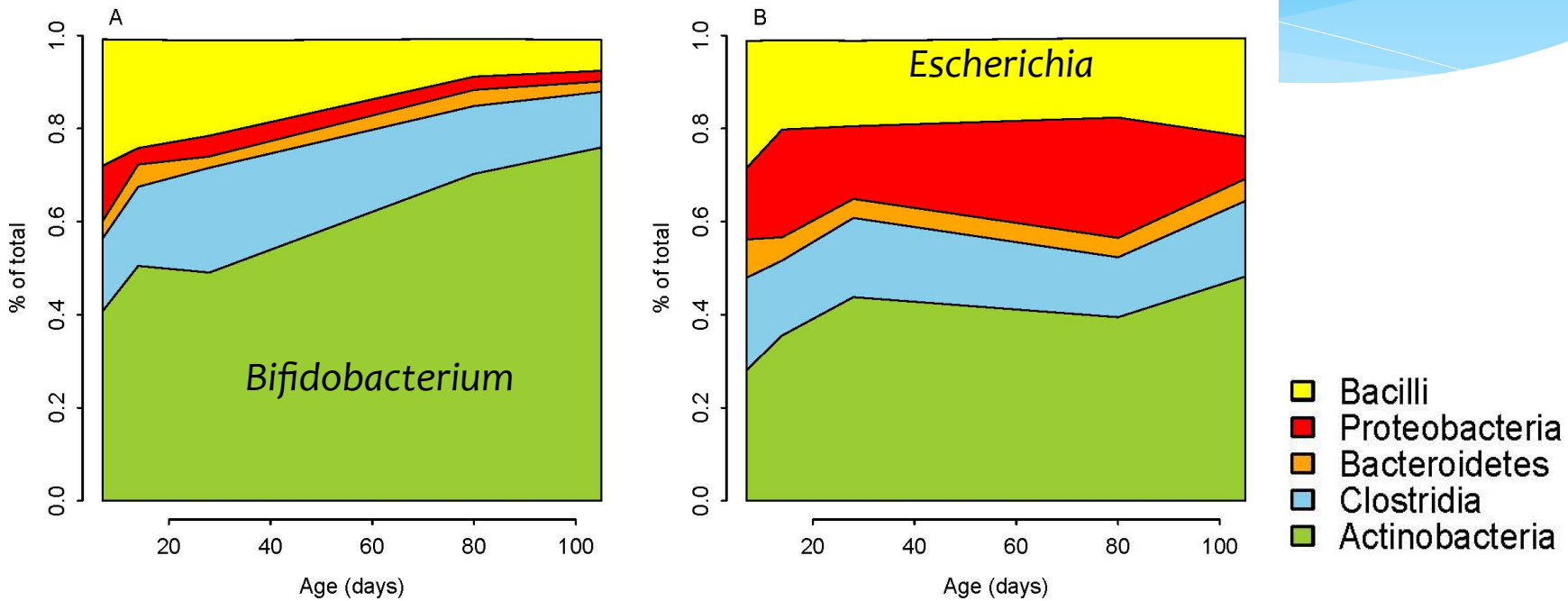


Weinig cortisol + weinig gerapporteerde stress
Gastrointestinale symptomen 22%
Allergische symptomen 0%

3

Maternal factors influencing development of the infant microbiota

Pamela D. Browne, Eva van den Berg, Eric Claassen, Carolina de Weerth



Weinig cortisol + weinig gerapporteerde stress
Gastrointestinale symptomen 22%
Allergische symptomen 0%

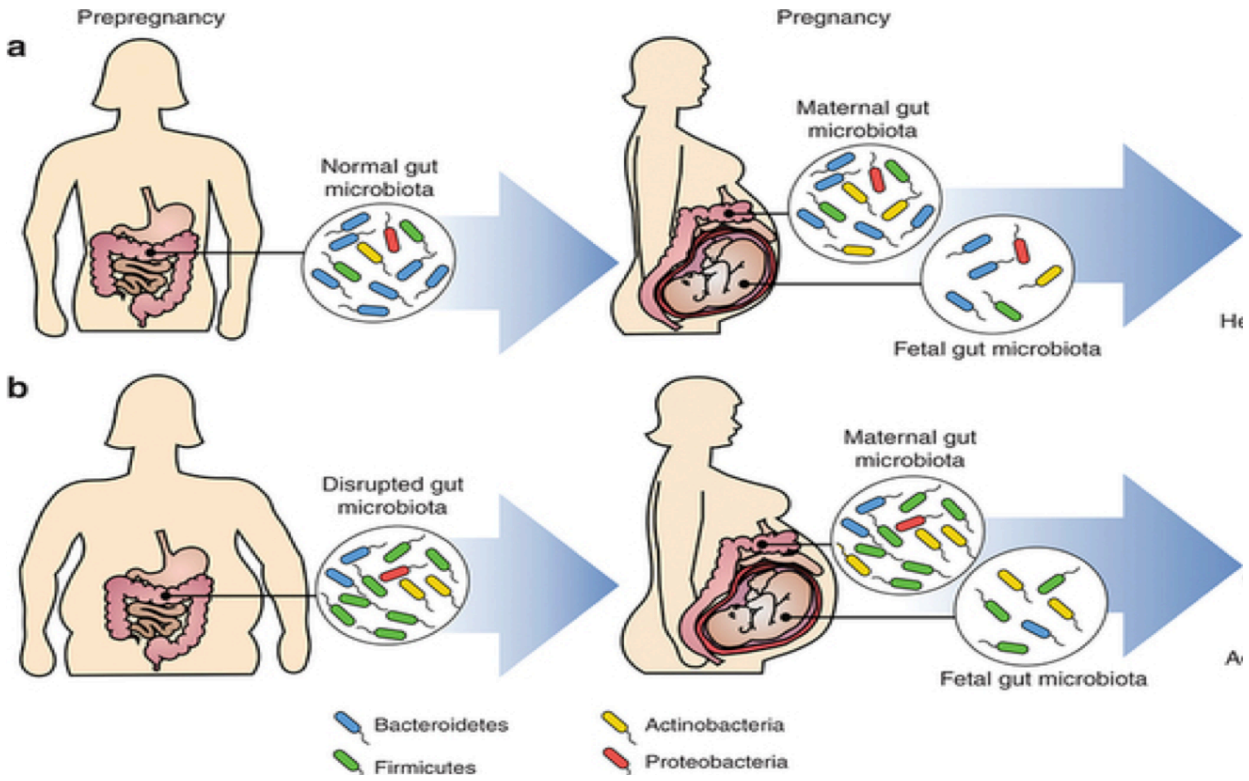
Veel cortisol + veel stress
Gastrointestinale symptomen 38%
Allergische symptomen 43%

Lange termijn!

- Verhoogd maternaal PNS → baby 30 dagen → 6 jaar

Zwangerschap: maternaal gewicht

Overgewicht beïnvloedt mogelijk darmbacteriën bij moeder en kind *Gohir, 2015*



Bifidobacterien,
Akkermansia

Clostridium,
Staphylococcus

The impact of pre and postnatal interventions on infant gut microbiota

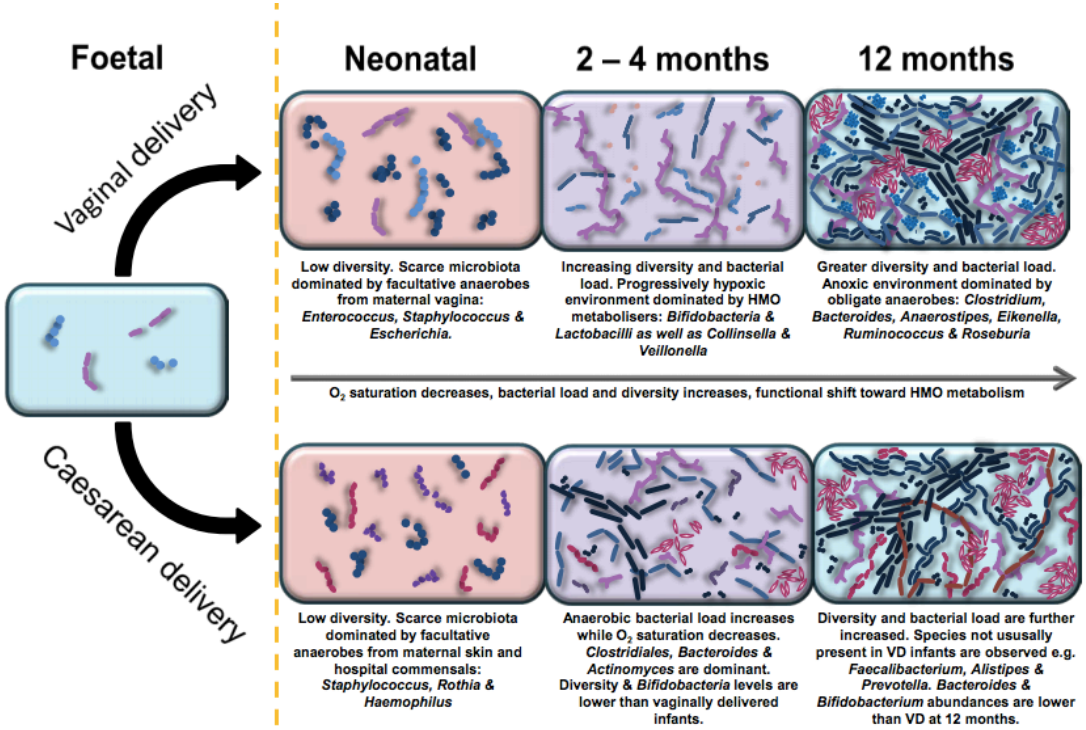
Anita Kozyrskyj, Mon Tun

- **Keizersnede** (spoed/electief)

o.a. verlate BV, AB gebruik

Genus: *Bacteroides*, diversiteit *Bacteroidetes* (4 mnd), bifidobacteria

Staphylococci, *C. difficile*



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- Meer risico atopische ziekten (eczeem, astma, allergieën), mogelijk overgewicht

4 The impact of pre and postnatal interventions on infant gut microbiota

Anita Kozyrskyj, Mon Tun

- **Maternaal antibiotica gebruik** (penicilline, gentamycine, ampillicine)
  - IV antibiotica (Groep B Streptococcen)
  - Lange termijn effecten microbiota kind onbekend, zwangerschapsduur afhankelijk

↓ Bifidobacteria, *B. fragilis*

↑ *Clostridium, Enterbacteriaceae (e.g. Klebsiella, E. Coli), Enterococcus, S. Aureus*

- **Ziekenhuis bevalling/hospitalisatie**
  - **2 dagen:** meer ***C. difficile***, minder *Bifidobacteriaceae*
  - **4-6 dagen:** 1 maand meer ***C. difficile,*** minder *Bifidobacteriaceae* en *B. fragilis*

- **Thuisbevalling**
  - Minder risico op astma 7 jaar bij kinderen met ouders met allergieën
  - Minder aanwezigheid ***C. difficile***

The impact of pre and postnatal interventions on infant gut microbiota

Anita Kozyrskyj, Mon Tun

- **Postnataal AB behandeling (> risico allergieën, astma, obesitas)**

  1. Na geboorte gentamicine, ampicilline (IV):
  minder bifidobacteria, lactobacillen, *Bacteroidetes*,
  meer *Proteobacterien*
  - tot 2 maanden zichtbaar na AB behandeling (meer *Proteobacterien;* < *Bifidobacterium* species)

  2. 1-3 maanden:
  Minder bifidobacteria, lactobacillen and *Bacteroides*
  Meer *Enterobacterien* Fallani *et al*., 2010

  3. 6 maanden:
  Ceftriaxone (5 dgn IV): totaal **minder** bacteriën, **geen** lactobacillen, **minder** *Enterobacteriaceae* en enterococci

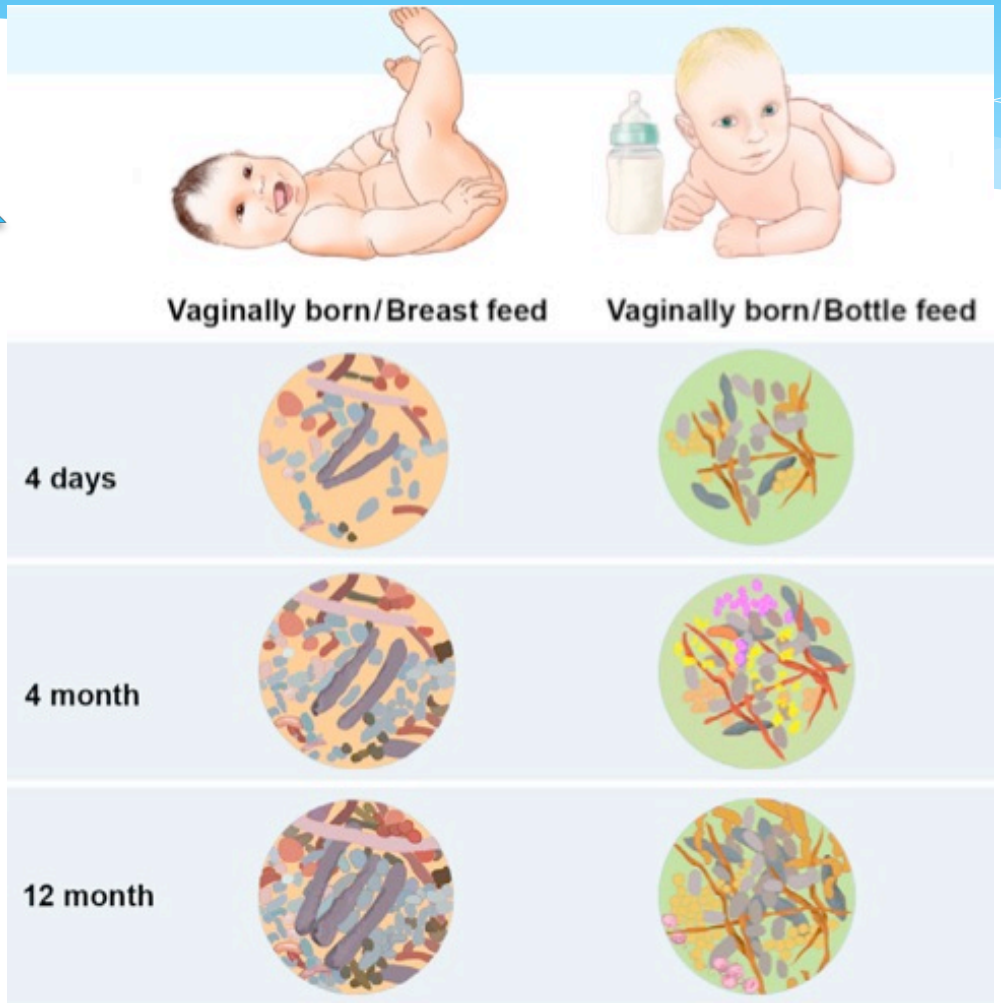
  4. 1-2 jaar:
  Amoxicilline (oraal): **minder** verschillende bifidobacterie stammen, evenveel bifido stammen

5 Early diet and the infant gut microbiome

John Penders

Bifidobacteria
lactobacilli
70-80%
Kashtanova *et al.*, 2016

Verteren borstvoeding suikers (HMO)



Sommige *Bifidobacterium* soorten
Bezirtzoglou *et al.*, 2011

***Bacteroides*, clostridia (*C. difficile*, *E. Coli*, *Enterobacteriaceae*)**

Grotere diversiteit

5 Early diet and the infant gut microbiome

John Penders

Key points en toekomst

1. Voeding

Flesvoeding

- *Of* en *evt. hoe* gerelateerd aan ziekten onbekend

Borstvoeding ++

- HMOs, Immuunglobulinen, voedingsstoffen
- Borstmelk microbioom helpt bij optimale kolonisatie

2. Weinig bekend over 'mixed feeding' en baby microbioom

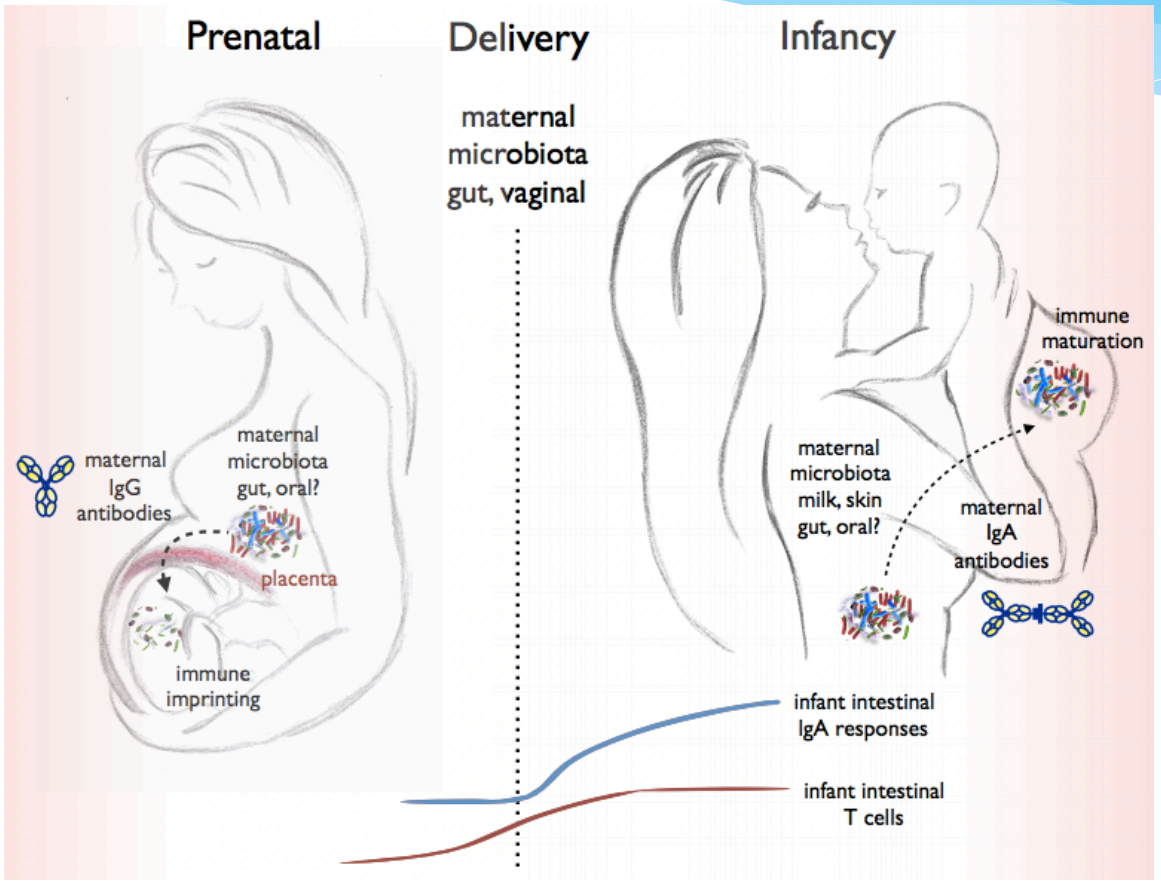
3. Stoppen borstvoeding, start vast voeding, of combinatie drijft maturatie naar volwassen microbioom?

4. Effect van moedermelk metabolieten/bioactieve stoffen apart op compositie van baby microbioom (gv. lactoferrine, lysozymen, immunoglobulinen, melk proteinen, lipiden)

6

The intestinal microbiota and the child's immune system

Maria C. Jenmalm, Susan L. Prescott



Immuun programmering

- IgG via placenta
- IgA via BV
- Mogelijke start *in utero*
- Intestinale B en T cellen foetus
  > 12-14 weken zwangerschap

6

The intestinal microbiota and the child's immune system

Maria C. Jenmalm, Susan L. Prescott

Key points:

- Microbiota primair signaal gezond functionerend intestinale barrière en immuunsysteem
- Omgeving tijdens zwangerschap mogelijk van invloed immuun maturatie (bv boerderij)

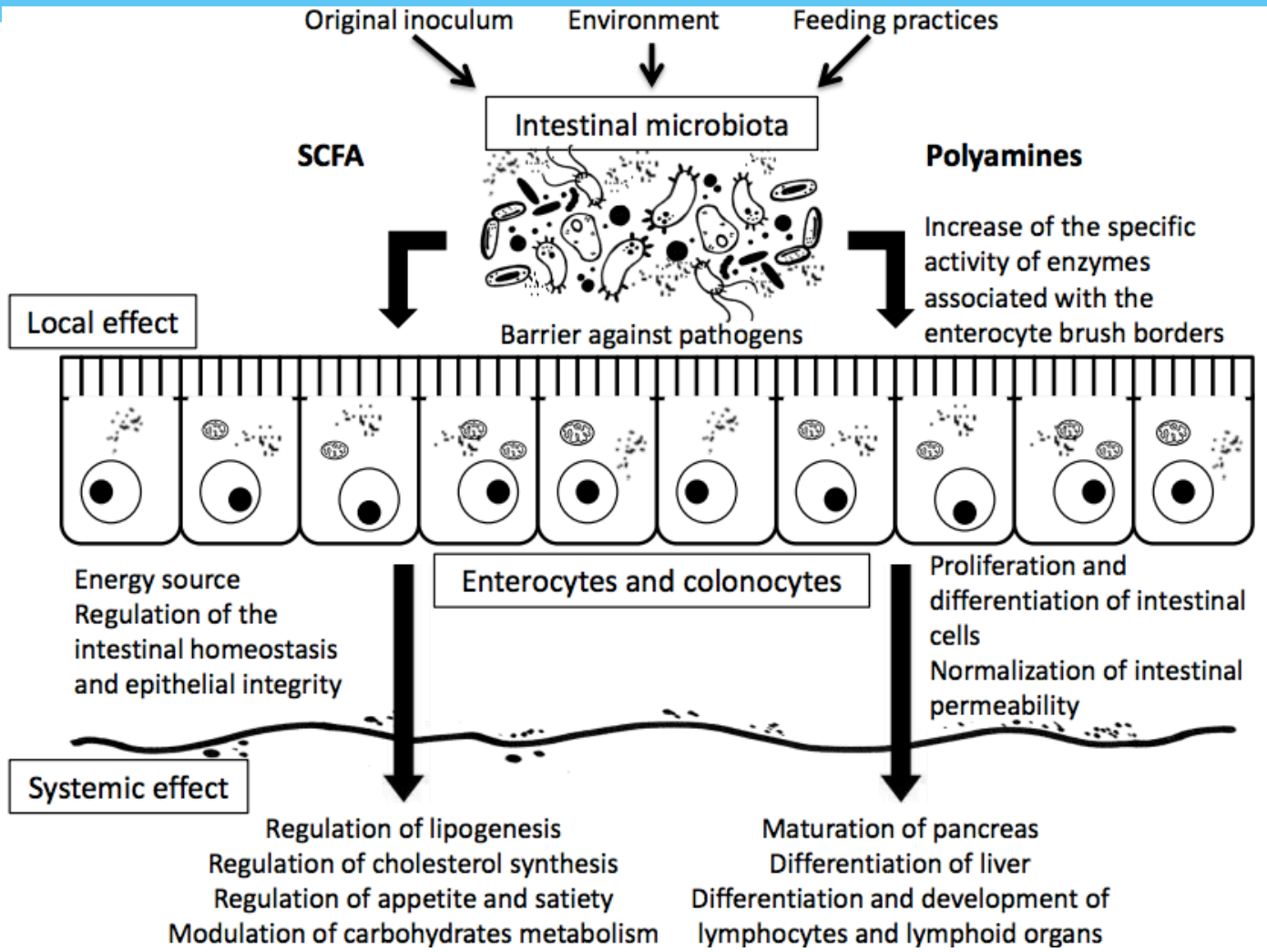
Toekomst:

- Grotere pediatrische cohorts met gedetailleerde immunologische en klinische uitkomstmaten

7

Interactions between intestinal microbiota and the gastrointestinal system

Carlos Gómez-Gallego, Seppo Salminen



Interactions between
intestinal microbiota and the gastrointestinal system

Carlos Gómez-Gallego, Seppo Salminen

Key points:

- Microbiota belangrijk maturatie gastro-intestinale stelsel (GE)
  - Verandering leefstijl, medische interventies → verandering microbioom + metabolieten → structurele veranderingen GE
- SCFAs en PAs belangrijk GE ontwikkeling

Toekomst:

- Definitie gezond intestinaal microbiota per persoon
  - Genetica, omgeving
- Gezondheid moeder, CS, perinataal AB gebruik: metabolieten?
- Meer informatie SCFAs profielen en PAs, om impact gedurende lactatie beter te begrijpen

8 The interplay between the microbiota and the central nervous system during neurodevelopment

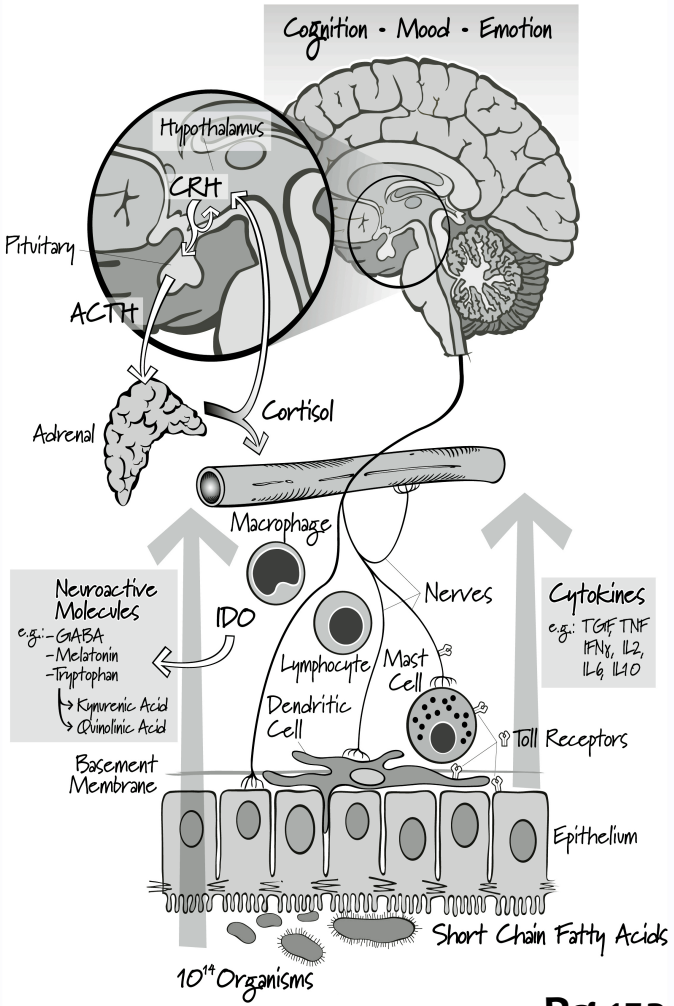
Aadil Bharwani, John Bienenstock, Paul Forsythe

Key points:

- Gut-brain axis: bidirectionaal via nervus vagus, immuunsysteem (cytokinen) en metabolieten (neurotransmitters)

- Bacterie stammen kunnen gedrag, emoties en cognitie beinvloeden
  - AB tijdens zwangerschap → afwijkende microbiota foetus en foetale neuronale ontwikkeling (muizen)

- ENS ontwikkeling: germ free →
  < ENS zenuw densiteit, < motiliteit, <zenuwen naar nervus vagus



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The interplay between the microbiota and the central nervous system during neurodevelopment

Aadil Bharwani, John Bienenstock, Paul Forsythe

Toekomst

- Welke signalen worden uitgezonden door microbiota, opgevangen door ENS, nervus vagus en immuunsysteem?
- Hoe worden signalen vanuit microbiota precies verwerkt in hersenen?

- 'Critical window of development'
  - Maternaal AB gebruik/maternaal stress/stress vroege leven, via microbiota, op neurologische ontwikkeling kind? Lange termijn en psychiatrische aandoeningen?

- MicroRNA (epitheel cellen) → innestelen darmbacteriën en mogelijk expressie beïnvloeden

- Dierstudies en *in vitro* modellen

9

The role of intestinal microbiota in infant allergic diseases

Hania Szajewska

Key points

- Microbiota kan immuunrespons beïnvloeden
- Afwijkende microbiota compositie jonge leeftijd (toename clostridia, afname bifidobacteria en diversiteit)
    - Eczeem, astma, allergieën, wheezing
- Rota vaccin respons gecorreleerd aan microbiota baby's (Harris, 2017)
- WAO richtlijnen

The role of intestinal microbiota in infant allergic diseases

Hania Szajewska

	World Allergy Organization (WAO) 2015 (probiotics) & 2016 (prebiotics)	European Academy of Allergy and Clinical Immunology 2014
Probiotics	Prevention of allergy • Evidence does not indicate that probiotic supplementation reduces the risk of developing allergy in children. Prevention of eczema • There is a likely net benefit from using probiotics. The WAO guideline panel suggests using probiotics in: 1. pregnant women at high risk* for having an allergic child; 2. women who breastfeed infants at high risk* of developing allergy; 3. infants at high risk* of developing allergy. (conditional recommendations; very low quality evidence).	There is no evidence to support the use of prebiotics or probiotics for food allergy prevention.
Prebiotics	The WAO guideline panel suggests: • using prebiotic supplementation in not-exclusively breastfed infants, both at high* and at low risk for developing allergy • not using prebiotic supplementation in exclusively breastfed infants. (conditional recommendations; very low quality evidence). : No recommendation about prebiotic supplementation during pregnancy or in breastfeeding mothers.	

*High risk was defined as the presence of a biologic parent or sibling with asthma, allergic rhinitis, eczema, or food allergy.

The role of intestinal microbiota in infant allergic diseases

Hania Szajewska

Toekomst

- Rol voor pre-probiotica ter preventie en behandeling allergieën.
- Grote langdurige RCTs om effectiviteit specifieke stammen te evalueren.
  Leidend tot advies *dosis, timing en duur* pre- of probiotica.
- Effectiviteit nieuwe pre- of probiotica stammen onderzoeken.

10

Intestinal microbiota and allergic and auto-immune disorders in children

Tim de Meij

Key points

- Effectiviteit behandelingen microbiota management bij IBD, IBS, coeliakie, DM1 bij kinderen teleurstellend
  - Oorzaak: te weinig bekend ziekte specifieke microbiota ‘signatures’
  - Patronen dysbiose verschillen
    - Afnemen monsters proefpersonen
    - Opslag
    - Analyse methoden

- IBD, IBS: VSL#3, studies kinderen<volwassenen
- Coeliakie, DM1/2: te weinig bewijs effectiviteit probiotica kinderen

10

Intestinal microbiota
and allergic and auto-immune disorders in children

Tim de Meij

Toekomst

- Microbiota mogelijk diagnostische biomarker ziekteactiviteit IBD, coeliakie, DM type 1
- Identificeren ziekte specifieke ‘signatures’ IBD, coeliakie, DM

11

Intestinal microbiota and the development of gastrointestinal disorders in children

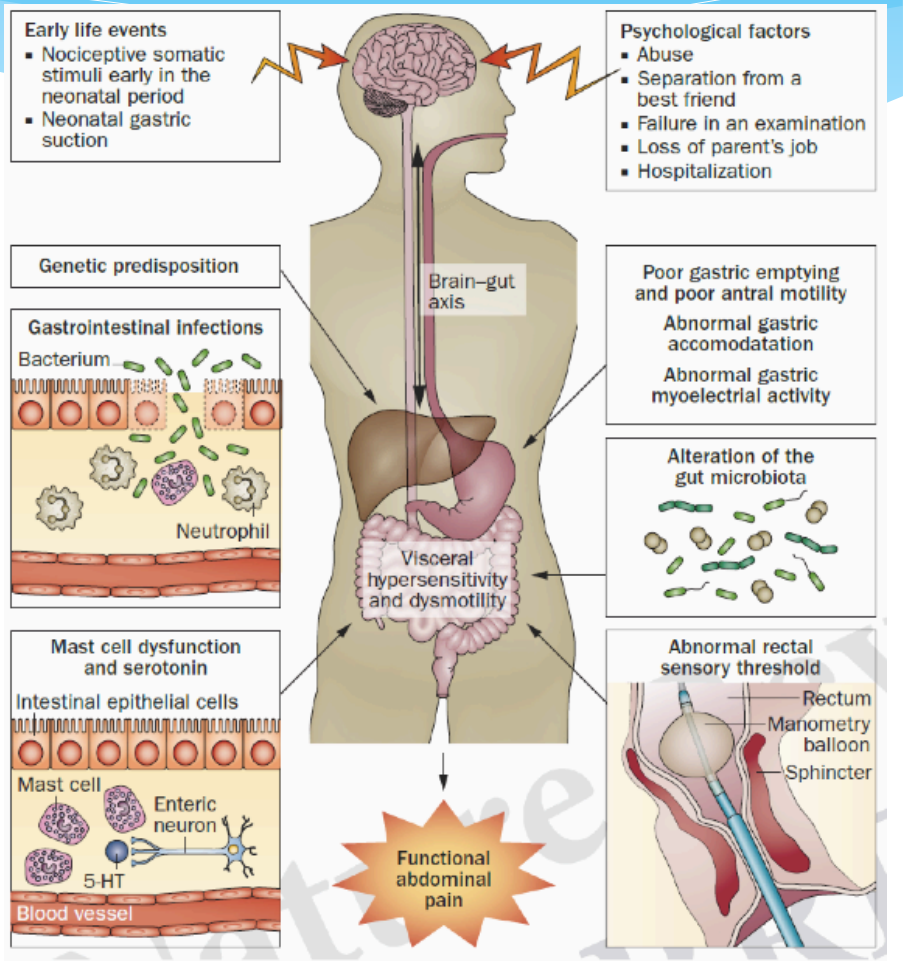
Marc A. Benninga, Marti Vink, L.M.A. Akkermans

Key points

- IBS/FAP/FC: rol voor probiotica
  - Motiliteit, frequentie, hardheid ontlasting
- Obesitas: teleurstellende lange termijn effecten probiotica gebruik

Toekomst

- Meer studies IBS/FAP/FC/infectieuze gastro-intestinale ziekten:
  - Voor bepalen optimale dosis, duur, stammen, combinatie van stammen



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12

The association between intestinal microbiota and infant crying and behaviour

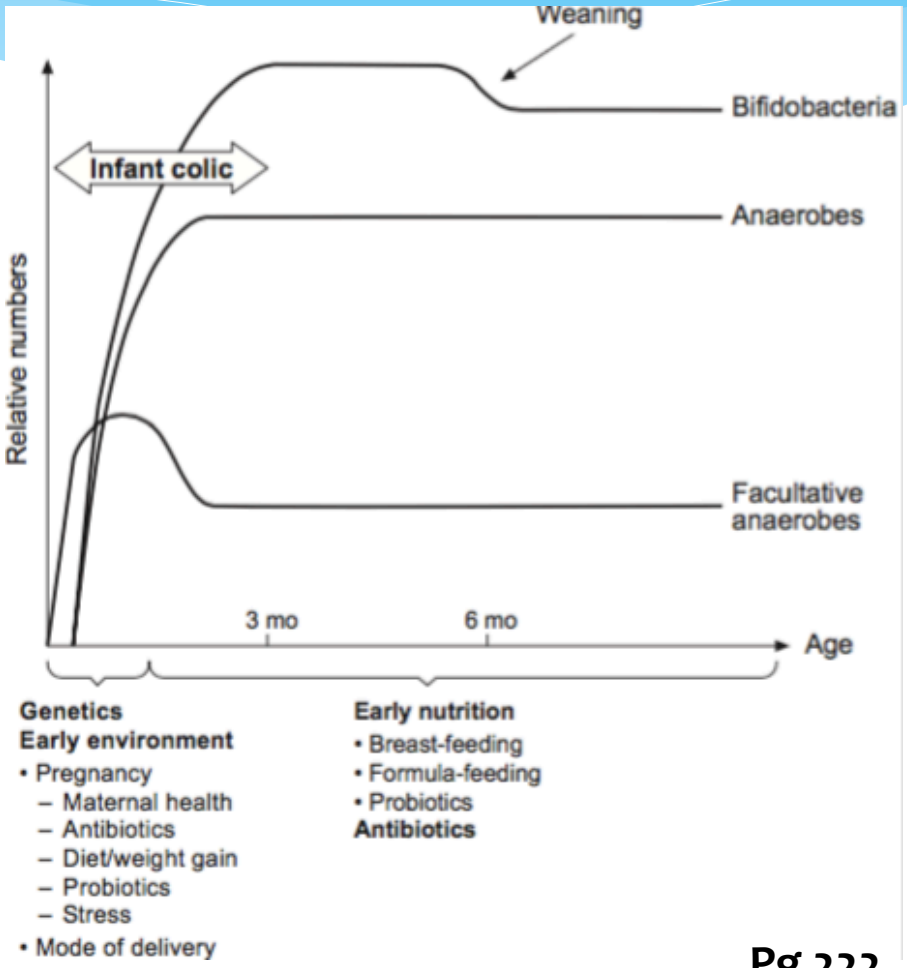
Valerie Sung, Anna Partty

Key points

- Probiotica (*L. Reuteri* DSM 17938) kan aanbevolen worden aan BV baby's, niet flesvoeding.

Toekomst

- Microbiota en inflammatoire veranderingen monitoren in probiotica studies
- Grote, kwalitatief goede, pragmatische clinical trials met gevalideerde uitkomstmaten
- Pooling data



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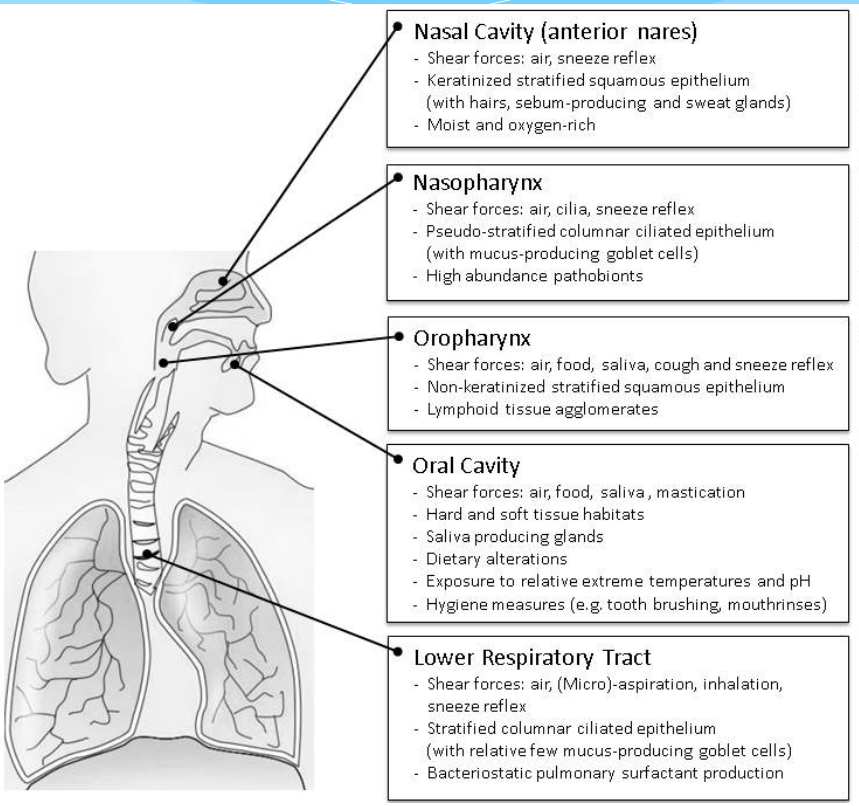
Microbiota and the respiratory tract

Jessica A. Younes, Jacoline Gerritsen

Key points

- Veel verschil microbiota verschillende niches
- Pathogenen vaak commensalen
- Respiratoire en orale ziekte: dysbiose in relatie met biofilms
- Kinderen met recidiverende oorinfecties mogelijk profijt van microbiota management therapieën



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Microbiota and the respiratory tract

Jessica A. Younes, Jacoline Gerritsen

Toekomst

- Meer onderzoek bij kinderen ipv volwassen met:

1) Polymicrobieel perspectief

2) Meer begrip ziek en gezond

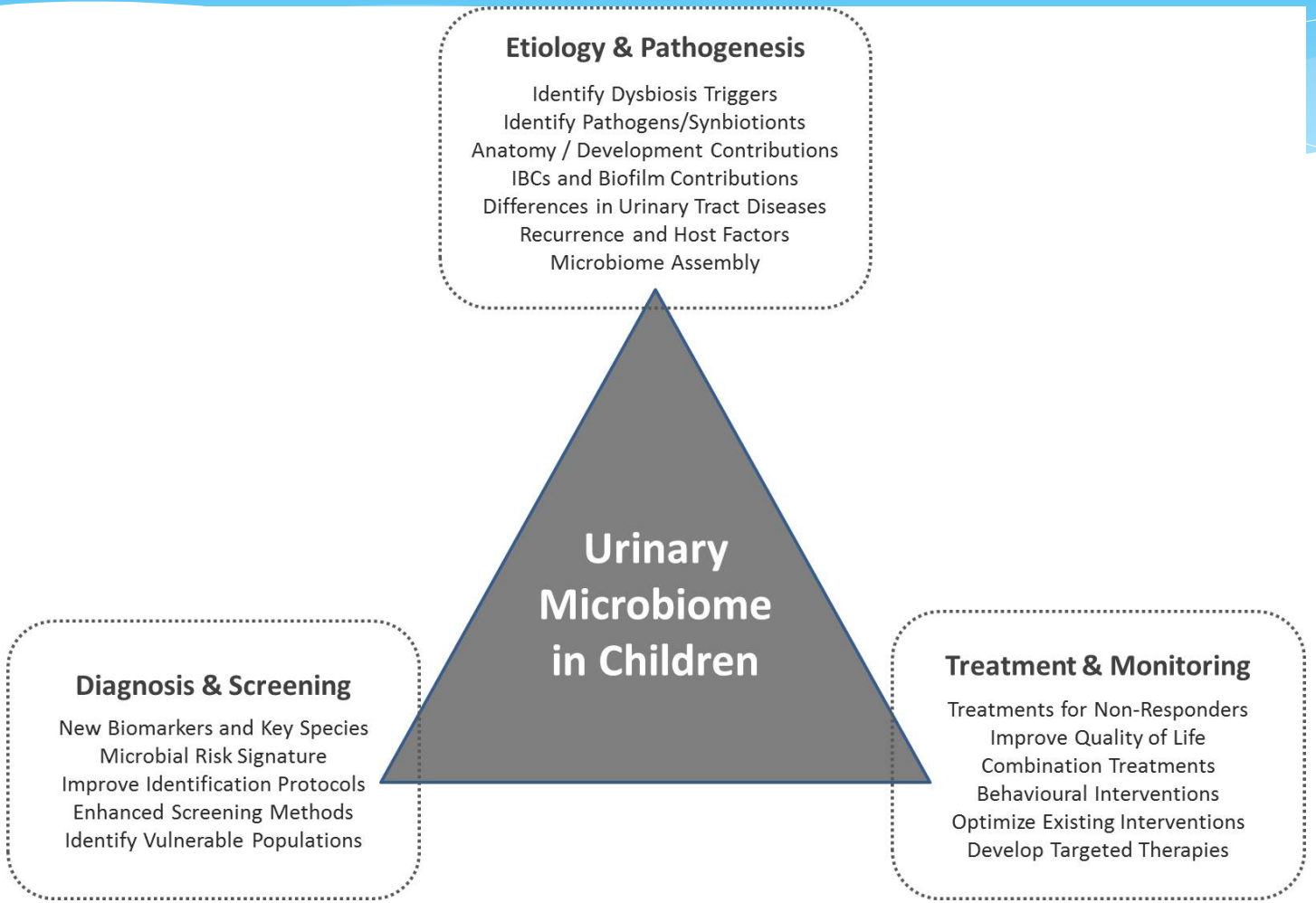
  - Idenficatie 'key species' in verschillende respiratoire en orale niches
  - Meer kennis van respiratoire en orale microbiota compositie
  - Meer kennis biofilm formatie en interactie met micro-organismen
  - Dysbiose → ziekte OF ziekte → dysbiose?
  - Meten activiteit/functionaliteit + drager reacties (e.g. epitheel gen expressie, immune cel activatie)

  - Meer kennis consequenties AB gebruik jonge leeftijd

14

Microbiota and the urinary system

Jessica A. Younes, Jacoline Gerritsen



14

Microbiota and the urinary system

Jessica A. Younes, Jacoline Gerritsen

Toekomst

- Karakteristieken ‘core microbiome’ in kinderblaas?
- Duur AB en meer risico profilering ter voorkoming lange profylaxe
- Microbiële blaas identificatie mogelijk?
- Beschermende factoren identificeren

15

Methodologies for microbiota assessment in infancy and childhood

D. Radjabzadeh, Sergey R. Konstantinov, Henriette A. Moll, André G. Uitterlinden, Erwin G. Zoetendal, Robert Kraaij

Key points

- Monsters zsm opslaan -80 gr C
- Duidelijke instructies + pictogrammen gebruiken collectie
- Analyse technieken laten aansluiten op onderzoeksvraag + populatie grootte

Toekomst

- Meer onderzoek: Archaea, viruses en fungi
- Van associatie naar causaliteit!

16

Probiotic interventions to optimize the infant and child microbiota

Yvan Vandenplas, Koen Huysentruyt

Key points

- Probiotica bij:
  - Gastro-enteritis
  - Respiratoire infecties
  - NEC
  - Eczeem
  - Infant colic, IBS
  - Oprispingen
  - AAD
  - *H. Pylori* infectie
  - (IBD/constipatie niet geïndiceerd bij kinderen)

16

Probiotic interventions to optimize the infant and child microbiota

Yvan Vandenplas, Koen Huysentruyt

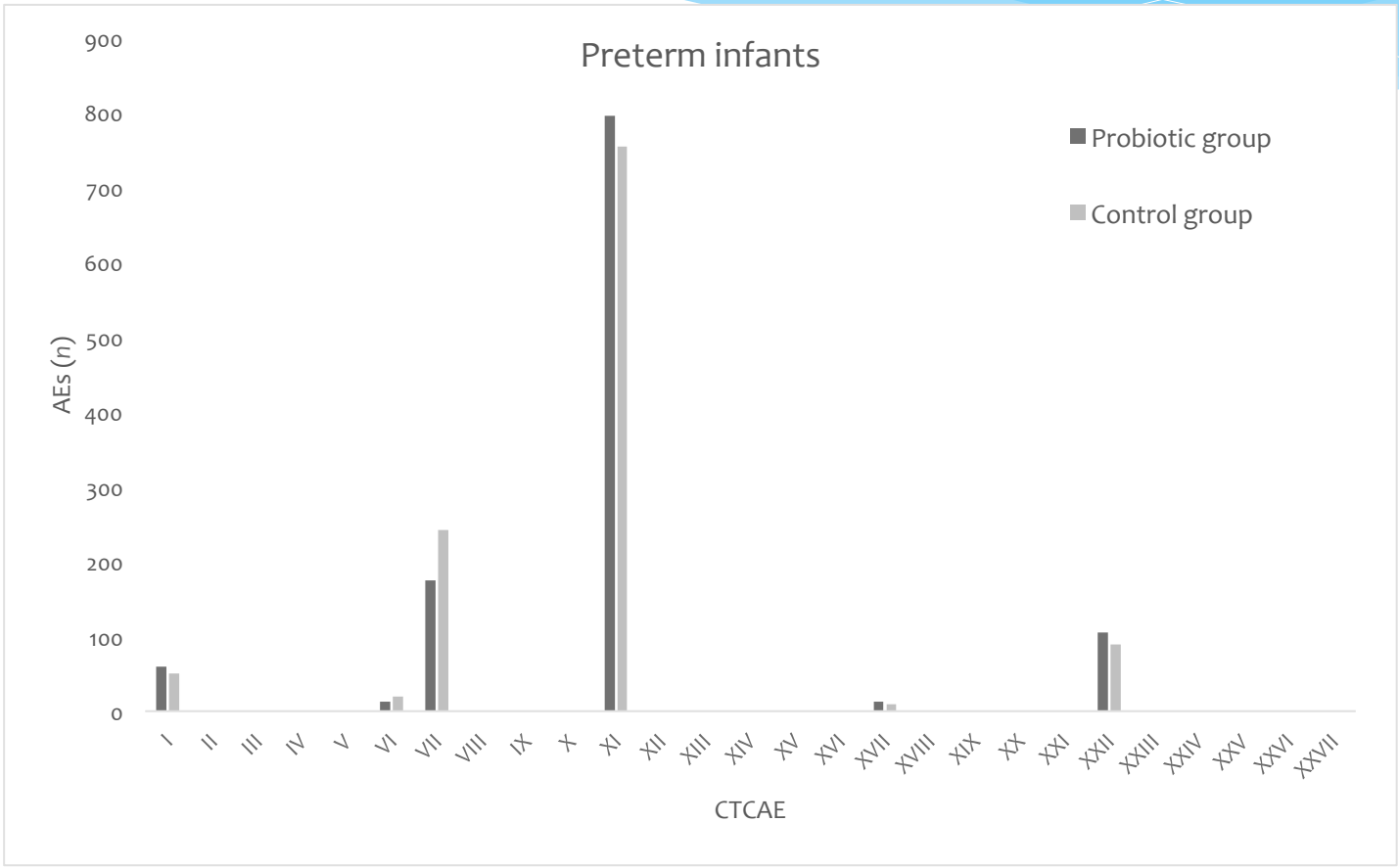
Toekomst

- Wat is een gezond gebalanceerd darmmicrobiota bij pasgeborenen?
- Rol (epi)genetica op darmmicrobiota compositie?
- Sprake van een ‘window of opportunity’?
- Hoe pre- en probiotica voorschrijven?

17

Safety of probiotics

Maurits van den Nieuwboer, Pamela D. Browne, Eric Claassen



17

Safety of probiotics

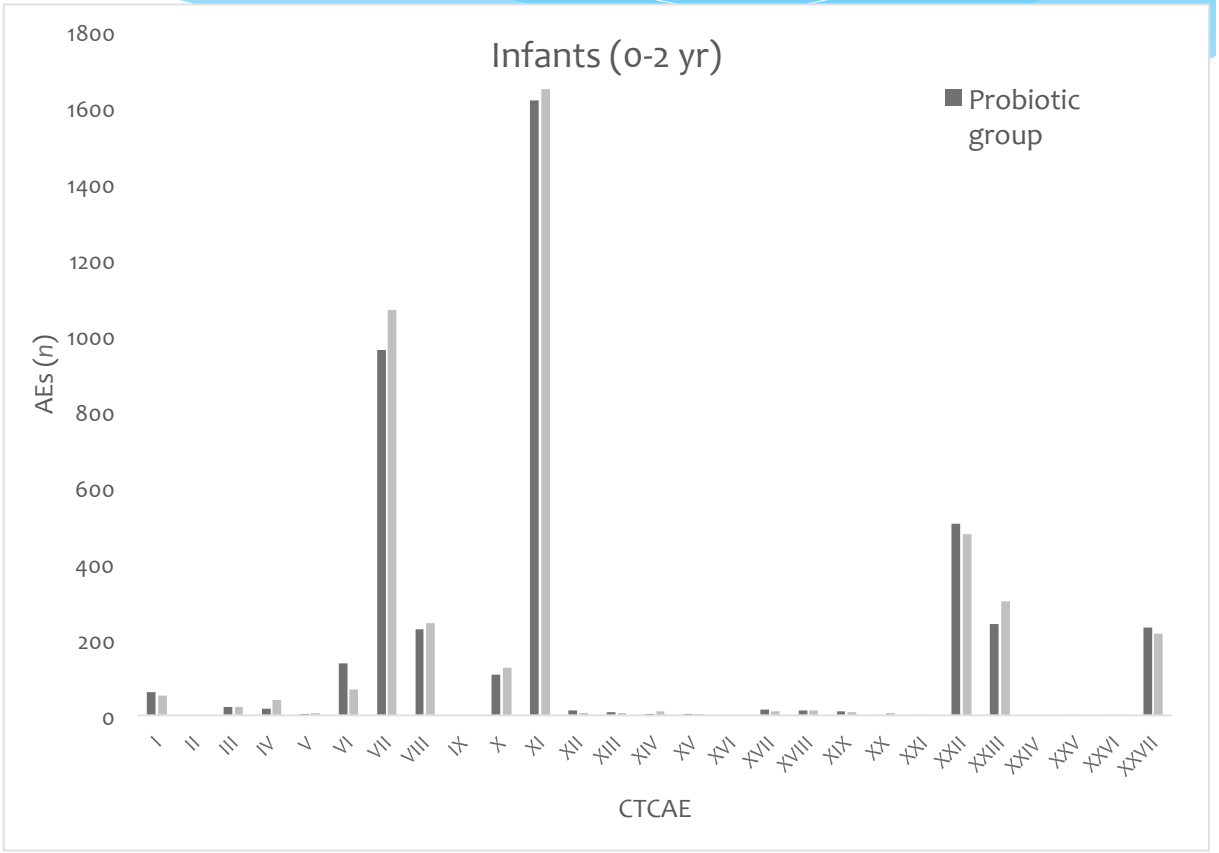
Maurits van den Nieuwboer, Pamela D. Browne, Eric Claassen

Key point

- Veilig baby's en tijdens zwangerschap

Toekomst

- Ziekte of behandeling **meer** bijwerkingen in controle groep



The infant and child microbiota

KEY MESSAGE

1 Priority in research should be identifying what constitutes a 'healthy, well-balanced' gastro-intestinal, respiratory and urinary microbiota composition during early life and childhood. **(Chapter 1)**

Maternal and external factors

KEY MESSAGES

1 Prenatal maternal factors, such as maternal psychosocial stress and maternal obesity can affect the infant microbial composition, which may adversely impact infant health. **(Chapter 3)**

2 Upon delivery, diet is one of the major factors impacting the maturation and diversification of the microbiome during early life. **(Chapter 5)**

3 Intrapartum antibiotic prophylaxis, hospitalisation post birth, perinatal treatment with antibiotics and elective or emergency caesarean delivery can cause pertubations in infant microbial composition, which may have long-term consequences on child health. **(Chapter 4)**

Digestive system

KEY MESSAGES

1 The first 18 months of life are considered crucial to the development of a healthy neonatal microbiota. **(Chapter 2)**

2 Proper preliminary colonisation seems necessary to maintain a fine balance between the members of the gut microbiota. Inadequate colonisation may lead to a state of dysbiosis, which can manifest in a number of disease states, including necrotising enterocolitis and neonatal sepsis. **(Chapter 2)**

3 Microbial metabolites such as short-chain fatty acids or polyamines may influence gastrointestinal functional development during early life. Thus, alterations in the microbial gut composition and activity of microbes may adversely affect gastrointestinal functioning with both short-term and long-term consequences on health. **(Chapter 7)**

4 Gut dysbiosis may be associated with functional abdominal pain (FAP) and functional constipation (FC). **(Chapter 11)**

5 The administration of probiotics, either as single treatment or as an adjuvant agent, may provide significant benefits for the treatment of infectious diseases caused by Escherichia coli, Clostridium difficile, Helicobacter Pylori and Shigella. Probiotics may be beneficial for treating functional gastrointestinal disorders and childhood obesity. **(Chapter 11)**

Immune system

KEY MESSAGES

1 The intestinal microbiota likely provides a primary signal for establishment of an adequate mucosal barrier function and the maturation of a balanced postnatal innate and adaptive immune system. **(Chapter 6)**

2 Early microbial exposures occurring during critical periods of immune maturation seem to have long-term impact on development of immune-mediated diseases, and the maternal microbial environment during pregnancy may also crucially influence immune programming. **(Chapter 6)**

3 The infant gut microbiota may influence the development of allergic diseases. Still, the role of gut microbiota in allergy has not been fully clarified. **(Chapter 9)**

4 Modifications of gut microbiota through the administration of probiotics, prebiotics and synbiotics could potentially play a role in the prevention and treatment of allergic diseases and eczema. **(Chapter 9 and 10)**

5 The intestinal microbiota may harbour potential as a diagnostic biomarker of disease and as a monitor of disease activity in inflammatory bowel disease, coeliac disease and type 1 diabetes in children. **(Chapter 10)**

Nervous system

KEY MESSAGES

1 There exists a compelling case for the role of gut microbiota in mediating CNS development, with downstream consequences on the shaping of behaviour, cognition, and neurodevelopment conditions. **(Chapter 8)**

2 Signalling along the gut-brain axis, even through single bacterial species, may alter the developmental trajectory of the stress circuitry and functional responses to stress. **(Chapter 8)**

3 Gut-brain signalling is complex and bidirectional, mediated through multiple candidate pathways that enable this interplay, including the vagus nerve, the immune system, and an array of metabolite mediators. **(Chapter 8)**

4 Accumulating evidence indicate interplay between gut microbiota, gut inflammation and the gut-brain axis in infants with colic. **(Chapter 12)**

5 Certain probiotic strains seem effective in treating infant colic in exclusively breastfed infants. **(Chapter 12)**

Respiratory system

KEY MESSAGES

1 Changes in local microbiomes have been associated with a growing number of inflammatory and infectious diseases of the respiratory tract and oral cavity during childhood. **(Chapter 13)**

2 Children that suffer from recurrent respiratory diseases may benefit from an early-stage intervention on a microbiome-level. **(Chapter 13)**

Urinary system

KEY MESSAGES

1 The bladder does not function as a sterile storage, instead live bacterial communities are present. **(Chapter 14)**

2 Evidence in adults suggests that UTIs in general are not caused by one or two pathogens, but rather might be a polymicrobial condition. **(Chapter 14)**

3 Certain pathogens have the ability to form intracellular bacterial communities with many biofilm-like properties, allowing bacteria to outlast a strong host immune response, and resist detection and antibiotic treatment. **(Chapter 14)**

Methodologies

KEY MESSAGE

1 Researchers should broaden their scope in microbiome research: additional focus on microorganisms, such as fungi, viruses, and niches outside the gut, including skin and urogenital microbiota. **(Chapter 15)**

2 The patterns of microbial dysbiosis in affected study subjects are often inconsistent, mainly due to differences in strategies regarding sample harvesting, collection and storage, and microbiota detection techniques. **(Chapter 10)**

Pre-, pro- and synbiotics

KEY MESSAGES

1 Pre-, pro- and synbiotics can be used for prevention and treatment of paediatric diseases, however, much remains unclear regarding optimal use of pre, pro- and synbiotics. **(Chapter 16)**

2 The probiotics used in clinical trials to reduce the risk of, prevent, or treat disease during perinatal period and childhood are considered safe for infants and children. **(Chapter 17)**

3 In human clinical trials, interventions with placebo products often result in more disease or treatment related side effects compared to treatment with probiotics. **(Chapter 17)**

SYMPOSIUM

SAVE THE DATE **November 30/2017**

MEDICAL BOOK SYMPOSIUM

Infant and Child Microbiota: From Pregnancy to Childhood

We kindly invite you to an evening of clinical learning about the 1st medical book worldwide published on the infant and child microbiotas.

REGISTRATION
Register on the website!
www.mylittlemicrobes.com

LOCATION
Landgoed Zonheuvel
Amersfoortseweg 98
3941 EP Doorn

My Little Microbes

This evening symposium will provide a clinical overview of the vital relationship between the microbiota and infant and child health. It offers the latest scientific findings on:
/ the interplay between gut microbiota and functional systems of body during infancy;
/ childhood diseases associated with dysbiosis;
/ the potential of microbial manipulation using pre- and probiotics.

Theoretical and practical talks, based on the the chapters of the book, will be given by world renowned experts in the field of pediatric microbiome research.

We look forward to welcoming you the 30th of November!
Drs. Pamela Browne (Vrije Universiteit Amsterdam)
Prof. dr. Eric Claassen (Vrije Universiteit Amsterdam)
Prof. dr. Michael Cabana (University of California, San Francisco)
Editors and organizing committee

SPONSORS

If interested in sponsoring, contact microbiomebook.falw@vu.nl

PROGRAM

16:00-16:30 **Registration and coffee**

16:30-16:40 **Book introduction and welcome address**

KEY NOTE LECTURES

16:40-17:25 **Prof. dr. Maria Jenmalm** Linköping University, Sweden
The intestinal microbiota and the child's immune system

17:25-18:10 **Prof. dr. Anita Kozyrskyj** University of Alberta, Canada
The impact of birth and postnatal medical interventions on infant gut microbiota

18:10-19:10 **Dinner**

19:10-19:55 **Prof. Dr. Hania Szajewska** Medical University of Warsaw, Poland
The role of intestinal microbiota in infant auto-immune and allergic diseases

19:55-20:40 **Dr. Koen Huysentruyt** Vrije Universiteit Brussel, Belgium
Probiotic interventions to optimise the infant and child microbiota

20:40-20:45 **Closing remarks**

20:45-21:30 **Drinks**

REGISTRATION
Please register at the symposium website before 12th November:
www.mylittlemicrobes.com

SYMPOSIUM REGISTRATION FEE
Includes: evening program, 3-course dinner and open bar
€ 45 (PhD students, non-physicians, physicians in training)
€ 80 (Medical specialists)

LOCATION
Landgoed Zonheuvel
Amersfoortseweg 98
3941 EP Doorn

Accreditation has been requested at the LHV, NVK, NVOG, V&VN en NVD.

Dank voor jullie aandacht!

Vragen?